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A SIMPLE ROUTE TO POLYCHLOROBENZIMIDAZOLES AND RELATED SYSTEMS

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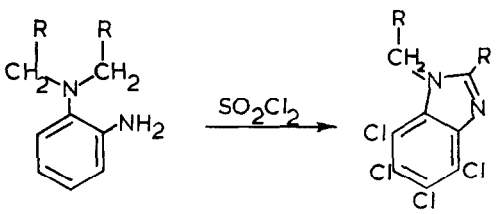
During attempts to prepare N-sulphonyl aniline derivatives ($PhN{=}SO_2$) we examined the interaction of sulphuryl chloride and o-aminodialkylanilines (1).



(1) (2)

a; R = H

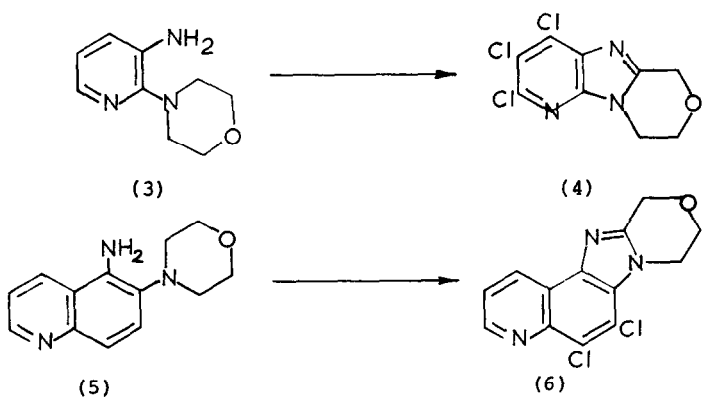
b; R - R = $(CH_2)_2$

c; R - R = $(CH_2)_3$

d; R - R = $(CH_2)_4$

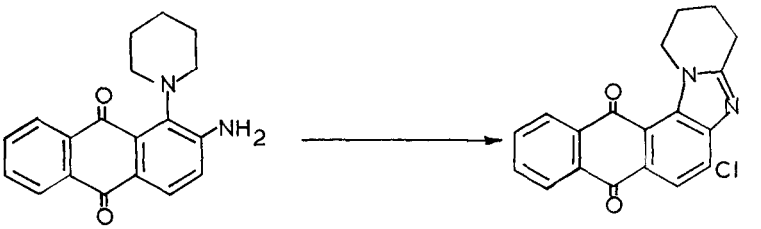
e; R - R = (CH_2OCH_2)

A remarkably vigorous, clean but non-exothermic, reaction occurs in the cold and in the absence of solvent, resulting in chlorination and cyclisation. In most cases, a good yield of the tetrachlorobenzimidazole (2) was isolated (Table). The product (2a) from o-dimethylaminoaniline (1a) was identical to that prepared by the four stage synthesis of Newbold and co-workers[1]. The procedure is equally applicable to the corresponding aminopyridine (3), -quinoline (5), and -anthraquinone (7), giving the analogous condensed imidazoles (4), (6)



(3) (4)

(5) (6)



(7) (8)

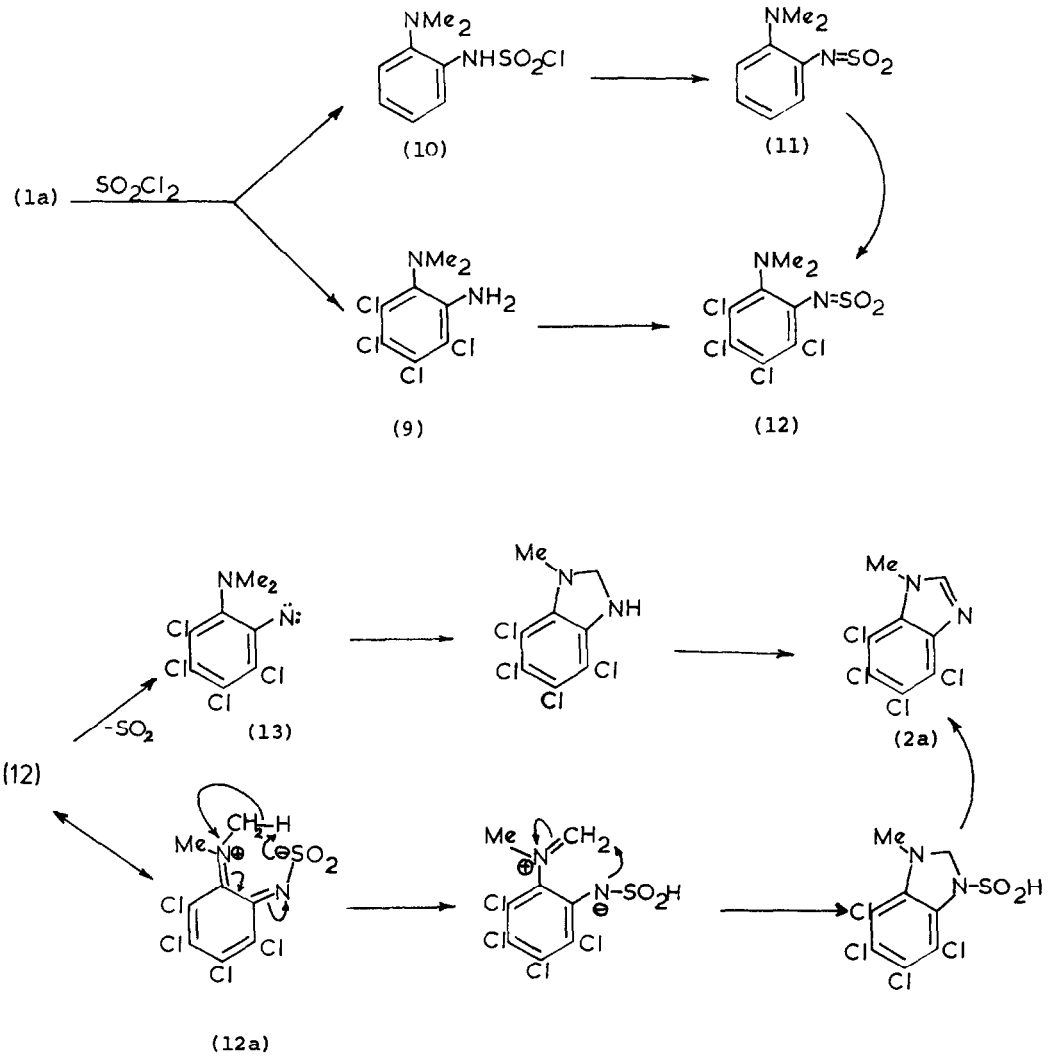
and (8). However, the o-aminophenylpyrrolidine (1b) gave a mixture of the corresponding mono-, di-, and trichlorobenzimidazole (cf. 2b).

We believe that the reaction initially follows two distinct pathways (Scheme), one yielding the sulphonylamine (11 or/and 12), while the other involves electrophilic chlorination of the highly activated aromatic nucleus. The subsequent cyclisation of the sulphonylamine to the benzimidazole may be envisaged to occur either by way of the nitrene

TABLE

Products derived from the action of SO_2Cl_2 on o-dialkylaminoarylamines

Starting Compound	Product	Yield(%)	M.p.	Remarks
1a	2a	50	255°	lit[1], m.p. 258-61°
1b	2b		131	mixture of mono-, di- and trichloro -derivatives
1c	2c	60	188	
1d	2d	85	232	
1e	2e	50	143	
3	4	40	243	
5	6	40	246	
7	8	40	269	

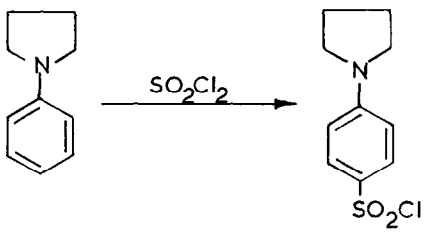


SCHEME

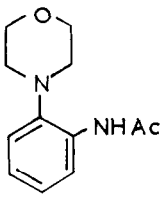
(13) (known to yield benzimidazoles[2]) produced by loss of SO_2, or by the intramolecular H-abstraction and cyclisation (via 12a), by analogy with numerous related cyclisations[3]. It appears that benzimidazole formation is slower than chlorination since the unchlorinated benzimidazoles give only a mixture of mono- and dichloro-derivatives on reaction with sulphuryl chloride. The fact that the pyrrolidine derivative (16) did not yield a fully chlorinated product (2b) would indicate that in this case the cyclisation step is more rapid than nuclear chlorination. This indirectly supports the second cyclisation mechanism

(12 → 12a) since we have found other examples in which the pyrrolidine derivatives are cyclised faster than the rest.

It is noteworthy that the N-phenyl-heterocycles (e.g., 13) give solely the corresponding sulphonyl chlorides (e.g., 14) under the above conditions, while the N-acetyl-



(13) (14)



(15)

derivative gave no benzimidazole (cf. 2) but a complex mixture of chlorinated products.

REFERENCES

1. D. E. Burton, A. J. Lambie, D. W. J. Lane, G. T. Newbold and A. Percival, J. Chem. Soc. (C), 1968, 1268.
2. O. Meth-Cohn, R. K. Smalley and H. Suschitzky, J. Chem. Soc., 1963, 1666
3. O. Meth-Cohn and H. Suschitzky, Advances in Heterocyclic Chemistry, 1972, 14, 211.